Comparative analysis of multiple myeloma treatment by CD138 antigen targeting with bismuth-213 and Melphalan chemotherapy.

Abstract:
Multiple myeloma (MM) is a B-cell malignancy of terminally differentiated plasma cells within the bone marrow. Despite intense research to develop new treatments, cure is almost never achieved. Alpha-radioimmunotherapy (RIT) has been shown to be effective in vivo in a MM model. In order to define where alpha-RIT stands in MM treatment, the aim of this study was to compare Melphalan, MM standard treatment, with alpha-RIT using a -anti-mCD138 antibody in a syngeneic mouse MM model. Methods: C57BL/KaLwRij mice were grafted with 1x106 5T33 murine MM cells. Luciferase transfected 5T33 were used for in vivo localization. The first step of the study was to assess the dose-response of Melphalan 21 days after engrafment. The second step consisted in therapeutic association: Melphalan followed by RIT at Day 22 and Day 25 after engraftment. Toxicity (animal weight, blood cell counts) and treatment efficacy were studied in animals receiving no treatment, injected with Melphalan alone, RIT alone at Day 22 and Day 25 (3.7MBq of -anti-CD138) and Melphalan combined with alpha-RIT. Results: Fifty percent of untreated mice died by Day 63 after MM engraftment. In mice treated with Melphalan alone, only the 200 μg dose improved median survival. No animal was cured after Melphalan treatment whereas 60% of the mice survived with RIT alone at Day 22 after tumor engraftment with only slight and reversible haematological radiotoxicity. No effect was observed with alpha-RIT 25 days after engraftment. Melphalan and alpha-RIT association does not improve overall survival compared to RIT alone, and results in increased leukocyte and red blood cell toxicity. Conclusions: Alpha-RIT seems to be a good alternative to Melphalan. Association of these two treatments provides no benefit. The perspectives of this work would be to evaluate RIT impact in the regimens incorporating the novel agents bortezomide, thalidomide and lenalidomide.


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